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YOUNG, SHAWQUIA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,362	MICHEL, DOMINIQUE	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,21-24 and 31-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *34 and 36-38* is/are allowed.

6)☒ Claim(s) *1,3-7,21-24,33,35 and 39* is/are rejected.

7)☒ Claim(s) *2,31,32 and 41-44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 21-24 and 31-44 are currently pending in the instant application. Applicants have cancelled claims 8 and 25 in an amendment filed on March 3, 2010. Claims 1, 3-7, 21-24, 33, 35 and 39 are rejected, claims 2, 31, 32 and 41-44 are objected and claims 34 and 36-38 are allowed in this Office Action.

I. *Response to Arguments*

Applicants arguments, filed March 3, 2010, relating to the rejection of claims 1, 3-7, 21-24, 33, 35 and 39 under 35 USC 103 as being unpatentable over Hill, et al. in view of Matsumoto have been fully considered but are not persuasive.

Applicants argue that the main difference from Applicants' process compared to Matsumoto is that applicant reacts primary amines at a pressure of 1.5 to 10bar. Applicants further argue that the claimed invention provides surprising and unexpected results. Applicants disclose that a primary amine with a formaldehyde source and a ketone gives, if at all, a secondary amine at a very low yield and a branched tertiary amine, wherein the primary amine is added twice to the formaldehyde source and a ketone, normally at low yields. Applicants also argue that the Differences between Applicant's claim 1 and the disclosure of Hill, et al. (even when Matsumoto is attempted to be added) is inventive, patentable and unexpected over Hill, et al because instant claim 1 is different by working under pressure of 1.5 to 10 bar. This difference in pressure surprisingly is sufficient to achieve a complete change in product composition from Hill, et al.

The Examiner wants point out that Applicants have provided an argument discussing the unexpected results of the claimed invention which is not sufficient to overcome the 103 rejection because as stated in MPEP 2145, "Arguments of counsel cannot take the place of factually supported objective evidence" and "A showing of unexpected results must be based on evidence, not argument or speculation". Therefore, Applicants are suggested to provide a declaration stating the unexpected results.

So in the absence of sufficient evidence showing the unexpected results of the Instant invention, the Examiner has maintained the position as stated in the Office Action mailed on August 31, 2009 that the "the secondary reference (Matsumoto) shows the use of high pressure in the mannich reaction of ketones and secondary amines is considered to be a powerful method and gives good yields even with sterically demanding effects. Since the only "critical" difference between the prior art and the instant invention is the use of pressure in the first step of the reaction process, the secondary reference shows that the use of pressure was already present in a similar type of reaction and the general reaction claimed by Applicants has been taught in the primary reference (Hill). Therefore combining the two references shows that it would have been obvious for Applicants to perform the first step in the claimed invention under pressure because a) the art teaches the general reaction and b) the art teaches the use of high pressure for the Mannich reaction" and that "the secondary reference shows that high pressure has been used in Mannich-type reactions which is what step(a) of Applicant's claimed invention is. The secondary reference shows that using high pressure is a "powerful method of aminomethylation and gives good yields". The use of high pressure in Mannich type reactions are known in the prior art. Applicants are modifying the reaction conditions of a known process (Hill, et al.) and according to In re Aller, modifying process conditions such as temperature and concentration is not a patentable modification absent a showing of criticality." Therefore, the Examiner has maintained the rejection of claims 1, 3-7, 21-24, 33 and 39 under 35 USC 103 rejection as being unpatentable over Hill, et al. in view of Matsumoto.

II. *Rejection(s)*

35 USC § 103 - OBVIOUSNESS REJECTION

The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

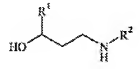
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). *See Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

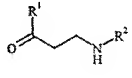
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-7, 21-24, 33, 35 and 39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Hill, et al.* in view of Matsumoto. Applicants claim The instant

invention claims a process for the preparation of a compound of formula



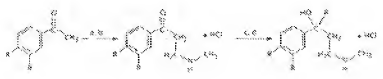
and/or an addition salt of a proton acid, wherein R^1 represents C_{1-8}-alkyl or phenyl and R^2 represents alkyl, cycloalkyl, aryl or aralkyl, each aryl or aralkyl being optionally further substituted with alkyl, alkoxy and/or halogen which process comprises the following steps: a) reacting a mixture comprising: (i) a methyl ketone of formula: CH_3COR^1 wherein R^1 is as defined above, and (ii) a compound of formula: $H_2N\text{-}R^2$ and/or an addition salt of proton acid, wherein R^2 is as defined above, and (iii) formaldehyde or a source of formaldehyde selected from the group consisting of formaldehyde in aqueous solution, 1,3,5-trioxane, paraformaldehyde and mixtures thereof, in the presence of a solvent selected from the group consisting of water, aliphatic alcohols, cycloaliphatic alcohols and mixtures thereof and optionally a proton acid to provide a β-keto amine of the formula



and/or an addition salt of a proton acid and b) reducing the carbonyl group of β-keto amine to afford a compound of formula I and/or an addition salt of a proton acid wherein the step a) is carried out at a pressure above 1.5 bar.

The Scope and Content of the Prior Art (MPEP §2141.01)

Hill, et al. teaches the following method



wherein a)$(HCHO)_n$, $MeNH_2$ HCl, EtOH, HCl, reflux; b) H_2O, steam distillation, MeOH; c) $NaBH_4$, 2-propanol/H_2O; d)MeOH, HCl; EtOH/Me_2CO; R is H or Cl.

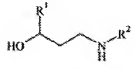
The secondary reference, *Matsumoto*, teaches the use of high pressure in the Mannich reaction of ketones and esters with dichloromethane and secondary amines. The secondary references teaches various reactions such as reacting $PhCOCH_2CH_3$ with $(Et)_2NH$ under high pressure.

The Difference Between the Prior Art and the Claims (MPEP §2141.02)

The difference between the prior art of *Hill, et al.* and the instant invention is that there is that step a) in the instant application is carried out at a pressure above 1.5 whereas in the prior art primary reference the first step is carried out under reflux and then steam distillation.

Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)

In In re Aller, 220 F.2d 454, 105 USPQ 233 (CCPA 1955), it was well established that merely modifying the process conditions such as temperature and concentration is not a patentable modification absent a showing of criticality. For example, it is obvious

to modify the preparation of a compound of  comprising step a) and step b) as disclosed in claim 1 to improve the product yield since a similar reaction using different conditions in step 1 was already taught by the primary reference and the use of high pressure in the Mannich reaction was taught by the secondary reference. Specifically, changing the reaction conditions of step 1 as seen in the claim 1 absent unexpected results is deemed obvious over the *Hill, et al.* reference in view of the secondary reference Matsumoto. The motivation for one of ordinary skill in the art to modify the first step of the prior art's reaction by using high pressure would be to develop a more efficient method for preparing amino alcohols. Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to attempt to improve the known process by modifying the reaction conditions (i.e. carrying out the first step under pressure) to increase the product yield when the secondary reference teaches the Mannich reaction of ketones and esters with dichloromethane and secondary amines under high pressure. A strong prima facie obviousness has been established.

III. *Objection(s)*

Dependent Claim Objections

Dependent Claims 2, 31, 32 and 41-44 are objected to as being dependent upon a rejected based claim. To overcome this objection, Applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim.

IV. Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626